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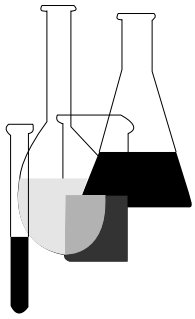
Occupational and Residential Exposure Test Guidelines

OPPTS 875.2000 Background for Postapplication Exposure Monitoring Test Guidelines



INTRODUCTION

This guideline is one of a series of test guidelines that have been developed by the Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency for use in the testing of pesticides and toxic substances, and the development of test data that must be submitted to the Agency for review under Federal regulations.

The Office of Prevention, Pesticides and Toxic Substances (OPPTS) has developed this guideline through a process of harmonization that blended the testing guidance and requirements that existed in the Office of Pollution Prevention and Toxics (OPPT) and appeared in Title 40, Chapter I, Subchapter R of the Code of Federal Regulations (CFR), the Office of Pesticide Programs (OPP) which appeared in publications of the National Technical Information Service (NTIS) and the guidelines published by the Organization for Economic Cooperation and Development (OECD).

The purpose of harmonizing these guidelines into a single set of OPPTS guidelines is to minimize variations among the testing procedures that must be performed to meet the data requirements of the U. S. Environmental Protection Agency under the Toxic Substances Control Act (15 U.S.C. 2601) and the Federal Insecticide, Fungicide and Rodenticide Act (7 U.S.C. 136, *et seq.*).

This guideline, along with the others in Series 875.2000 through 875.2900, is being substantially revised for publication in 1997. However, the current guidelines are still official. Before initiating any studies for post-application exposure registrants should contact EPA's Occupational and Residential Exposure Branch (within the Office of Pesticide Programs) at 703–305–6094.

Final Guideline Release: This guideline is available from the U.S. Government Printing Office, Washington, DC 20402 on *The Federal Bulletin Board*. By modem dial 202–512–1387, telnet and ftp: fedbbs.access.gpo.gov (IP 162.140.64.19), internet: http://fedbbs.access.gpo.gov, or call 202–512–0132 for disks or paper copies. This guideline is also available electronically in ASCII and PDF (portable document format) from the EPA Public Access Gopher (gopher.epa.gov) under the heading ''Environmental Test Methods and Guidelines.''

OPPTS 875.2000 Background for postapplication exposure monitoring test guidelines.

(a) **Scope**—(1) **Applicability.** This guideline is intended to meet testing requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136, *et seq.*).

(2) **Background.** The source material used in developing this harmonized OPPTS test guideline are OPP guidelines 130 and 131.

(b) **General provisions**—(1) **Basic guidance**—(i) **Purpose.** (A) This series describes the requirements of 40 CFR 158.390 for registration support data which the Agency will evaluate in order to determine what label restrictions, if any, are needed to protect people who enter a site which has been treated with a pesticide. Human protection through minimization of human exposure to pesticide residues is the purpose of 40 CFR 158.390 and this guideline. The Agency requirements for data required by 40 CFR 158.390 will be based upon:

(*1*) Determination of the time necessary for pesticide residues at the treated site to decline to an allowable reentry level (a level which will not be hazardous to humans).

(*2*) Placement of a reentry interval (interval during which no entry to the treated site should routinely be permitted) on a pesticide label.

(*3*) Judgment as to the utility, availability, and likelihood of use of personal protective equipment to be used by people entering a treated site.

(B) The reentry level is a level of pesticide residues in the environment which will not cause unreasonable adverse health effects in people entering a treated site without use of personal protective equipment. The reentry interval is the time it takes for the pesticide residues to dissipate to the reentry level. Use of personal protective equipment and other measures will be required, when it is necessary for people to enter a site before the pesticide residues have dissipated to the reentry level.

(C) Data necessary to determine reentry levels and reentry intervals include:

(*1*) Data on toxicity of the pesticide.

(*2*) Data on expected human exposure to the pesticide residues from typical human activities that would take place at a site that has been treated with a pesticide.

(*3*) Data on the nature and amount of pesticide residues remaining at the treated site (on foliage, soil, or other surfaces and in the air).

(ii) **Use of reentry interval.** The applicant should submit a label for the prospective product which will include a proposed reentry interval.

This proposed interval is to be supported by data required by 40 CFR 158.390 and described under paragraph (b)(2) of this guideline. The Agency will review the data and accept or reject the proposed interval.

(iii) **Application status and compliance.** The requirements of 40 CFR 158.390 apply to products already registered, as well as those being proposed for registration. The Agency will notify registrants of products already registered, either (occasionally) through the data call-in program or (routinely) upon development of a registration standard, as to when they must satisfy the data requirements of this guideline. Refer to 40 CFR part 158 for details on application status in relation to submittal times.

(iv) **General references.** Information concerning the history of the reentry problem, the present state of the art, recent experimental activity, and suggested approaches to reentry assessment can be found under paragraphs (i)(3), (i)(10), and (i)(12) of this guideline.

(2) **Requirement for reentry interval and supporting data.** (i) A reentry interval and the supporting data discussed in this series are required by 40 CFR 158.390 to support the registration of each end-use product that meets one or more of the toxicity criteria and that has a use type that could be included in the use classifications specified:

(A) Toxicity criteria. If the pesticide toxicity data meet one or more of the following criteria based on toxicity studies required under 40 CFR 158.135, then a reentry interval and supporting data are required:

(*1*) If the LD50 of the technical grade of any active ingredient in the end-use product is less than 200 mg/kg (body weight) as determined by acute dermal toxicity testing (OPPTS 870.1200).

(*2*) If the LC50 of the technical grade of any active ingredient in the end-use product is less than 200 mg/m3 (for a one-hour exposure) as determined by acute inhalation toxicity testing (OPPTS 870.1300).

(*3*) If the LD50 of the technical grade of any active ingredient in the end-use product is less than 50 mg/kg (body weight) as determined by acute oral toxicity testing (OPPTS 880.1100).

(*4*) If neurotoxic, teratogenic, or oncogenic effects, as evidenced by studies conducted in accordance with OPPTS 870.6100, 870.4200, 870.3200, or other adverse effects as evidenced by subchronic, chronic, and reproduction studies conducted in accordance with OPPTS 870.3100, 870.3150, 870.3200, 870.3250, 870.3465, 870.3800, and 870.4100 would be expected from entry of persons into treated sites, taking into account the pattern and frequency of pesticide use and the results of a risk analysis based on margins of safety or derived from mathematical models according to paragraph (f)(3) of this guideline.

(*5*) If the Agency receives other scientifically validated toxicological or epidemiological evidence that a pesticide or residue of a pesticide could cause adverse effects to persons entering treated sites. In this situation, reentry intervals and supporting data may be required on a case-by-case basis.

(B) Use types. The following pesticide use types are subject to the requirement for submittal of proposed reentry intervals and the corresponding data:

(*1*) Applications to growing crops, such as typical applications of insecticides, fungicides, and herbicides made to or around all horticultural and agronomic crops that are field- or orchardgrown.

(*2*) Uses of pesticides to all outdoor tree nursery and forestry operations.

(*3*) Applications to turf crops and commercial applications to turf.

(*4*) Applications to parks and arboretums.

(ii) Waivers. (A) General waiver. Applicants for registration may request a waiver from the requirement to submit some or all of the data required by 40 CFR 158.390 provided that they submit written evidence that such data are inapplicable to the specific pesticide or product. (See also 40 CFR 158.45.)

(B) Waiver for no substantial exposure. Applicants may provide a description of sites and human reentry activities (see OPPTS 875.2800) revealing that no substantial human exposure to pesticide residues can be reasonably foreseen. If an applicant also requests a waiver from the requirement to provide a reentry interval on a particular product label, the Agency will review the request and the descriptions submitted. If the Agency agrees with the submitted rationale, it will grant a waiver.

(C) Waiver for other specific reasons. Applicants may request a waiver from submittal of certain data required by 40 CFR 158.390 and discussed in this guideline, if they submit evidence that specific properties or characteristics of the pesticide or product preclude the requirement for such data. Such properties or characteristics could include, but are not limited to, the composition, degradation rate, toxicity, and such other chemical and physical properties of a specific pesticide or product that are fundamentally different from the factors considered by the Agency in the establishment of the data requirements of 40 CFR 158.390.

(iii) Exposure only to airborne residues covered by other regulations. In the case of reentry to a site which is expected to involve only exposures to airborne residues which are covered by the Permissible Exposure Limits developed by the Occupational Safety and Health Administration (29 CFR 1910.1000) or the Threshold Limit Values (TLV) developed by the Amer-

ican Conference of Governmental Industrial Hygienists (ACGIH), those limits may serve as reentry levels for airborne residues and can be used by a registrant for determination of a proposed reentry interval.

(c) **Definitions.** Terms used in this guideline have the meanings set forth at 40 CFR l52.3 and at 40 CFR part 158. In addition, for the purposes of this guideline:

Airborne residue means residue of a pesticide, including vapors, aerosols, and airborne particulates, that remains become suspended in the air at a treated site during a normal human activity.

Allowable exposure level (AEL) means the maximum amount of combined dermal and inhalation exposure which is considered not to cause unreasonable adverse effects to people entering a previously treated site. An AEL will generally be based on animal toxicity studies and adjusted by means of an appropriate safety factor.

Dermal exposure means the process by which pesticide residues are deposited on the skin of people entering a previously-treated site. The term also refers to a measure of the amount of residue deposited by such exposure. It is synonymous with the external dermal exposure, and it is not necessarily equivalent to the amount of residue which would be absorbed into the body through the skin.

Direct exposure method means a procedure for measuring the quantity of pesticide residue transferred to a person's skin or respiratory tract. This method would involve, but not be limited to, measuring residues on dermal patches or respirator filters. This method excludes indirect exposure methods, such as quantification of pesticide residues in blood, urine, or tissues, and excludes measurement of physiological changes, such as changes of blood enzyme activities.

Dislodgeable residue means that portion of pesticide residue on a surface that can be dislodged from that surface by human activities involving contact with the surface. The term also includes residue that can be dislodged by dissolving in moisture (dew, rain, perspiration) and which then can contaminate skin, respiratory tissues, hair, clothing, etc., of people entering the treated site. The surfaces involved include, but are not limited to, foliage, agricultural produce, and soils.

Dissipation curve means a plot of the logarithm ofpesticide residue level against time of sampling, or the mathematical representation of such a plot.

Early reentry means the entry of people into a site previously treated with a pesticide prior to expiration of any established, pertinent reentry interval.

Inhalation exposure means the process by which pesticide residues are inhaled by a person in a treated site. The term also refers to the quantity of residue sorbed by respiratory tissues by such a process. This term is synonymous with pulmonary or respiratory exposure, and is not necessarily equivalent to the amount of residue which would be absorbed into the body through the pulmonary system.

Personal protective equipment means special clothing, hats, shoes, gloves, respirators, or other devices attached to or covering people and intended to reduce human exposure to pesticide residues. This term refers to items that normally would not be used in the absence of pesticide hazards and that would provide greater protection to people than normal attire.

Proposed reentry interval means a reentry interval proposed by an applicant as adequate for human protection.

Reentry means the entry of one or more people into a site subsequent to pesticide application.

Reentry interval means the length of time that must elapse after pesticide application before people who are not using personal protective equipment may enter the treated site without risk of any unreasonable adverse effects due to exposure to pesticide residues.

Reentry level means the maximum level of pesticideresidues at a treated site that is not likely to pose unreasonable adverse affects on people entering the site without personal protective equipment.

Residue, pesticide residue, and residue of a pesticide mean active ingredients, toxic impurities of the pesticide, and toxic alteration products of the active ingredient that remain at the site of application or that remain on items that are subsequently removed from the site.

Site means a specific agricultural area such as a field, grove, vineyard, or orchard.

Surrogate, *surrogate of a pesticide*, or *pesticide surrogate* means a chemical compound or a mixture of compounds other than the pesticide being investigated which could be used to quantify human exposure. The surrogate could be an active ingredient of a pesticide previously registered for that use.

Task means a human work activity performed according to current commonly-recognized practice or any other human activity that could cause exposure to pesticide residues at the site.

Typical end-use product means a pesticide product that is representative of a major formulation category (e.g., emulsifiable concentrate, granular product, wettable powder) and contains the active ingredient of the registration applicant’s product.

(d) **General reporting requirements**—(1) **General.** Each test report submitted to meet the requirements of 40 CFR 158.390 should include the following information specified in paragraphs (b) and (f) of this guideline, specific section elsewhere in this guideline indicates otherwise. The registration applicant should remember that standardization of data reporting and submission of a complete report will expedite the review process. Multipurpose data should be referenced to specific pages in other volumes or be duplicated and submitted in each appropriate volume.

(2) **Test report.** The test report should include all information necessary to provide a complete and accurate description of test procedures, materials, results, and analysis of the data, a statement of conclusions drawn from the analyses, and a tabular summary and abstract of results. Units of measurement should be in the metric system, but the English system may be used in addition. The two systems may not be mixed (e.g., g/ft^2). The statement of test methods used should include a full description of the experimental design, the sites or locations, duration, and actual dates of the study.

(3) **Deviation.** The report should indicate all ways in which the test procedure failed to meet applicable standards for acceptable testing contained in this guideline, and should state the reasons for such deviations.

(4) **Test substance.** (i) The test substance should be identified, including chemical name, molecular structure, and a quantitative and qualitative determination of its chemical composition (including names and quantities of known contaminants and impurities, so far as technically feasible). The determinations should also include quantities of unknown materials, if any, so that 100 percent of the sample tested is accounted for. This information would ordinarily be developed to meet the requirements of 40 CFR 158.150 discussed in OPPTS Series 830.

(ii) Manufacturer and lot and sample numbers of the test substance should be reported.

(e) **Coordination with other requirements in 40 CFR part 158.** Applicants should determine whether studies conducted to meet the requirements of 40 CFR 158.390 can be coordinated with studies required by other sections of 40 CFR part 158 (such as OPPTS 830.1600); § 158.540 in OPPTS Series 850 (Hazard Evaluation: Nontarget Target Plants); § 158.290 in OPPTS Series 835 (Chemistry Requirements: Environmental Fate), and § 158.240 in OPPTS Series 860 (Chemistry Requirements: Residue Chemistry). The studies should be coordinated with the data gathered to meet the requirements of 40 CFR 158.340 in OPPTS Series 870 (Hazard Evaluation: Humans and Domestic Animals). In addition, some of the studies might be usefully coordinated with those required for supporting a tolerance or temporary tolerance petition under the Federal Food, Drug and Cosmetic Act (21 U.S.C. 408 and 409).

(f) **Toxicity data required.** The toxicological data submitted by registration applicants to evaluate the toxicity of a pesticide to humans and domestic animals as required by 40 CFR 158.340 should be used to determine an AEL for use in proposing reentry intervals. Those data are described in OPPTS Series 870, Groups A through F.

(g) **Exposure conversions and penetration assumptions**—(1) **General procedure.** (i) The AEL should be determined by the applicant from either:

(A) Animal dermal and/or inhalation toxicity data from acute and subchronic studies conducted to meet the requirements of 40 CFR 158.340, as described in OPPTS guidelines 870.1200, 870.1300, 870.1200, 870.3200, 870.3250, and 870.2400).

(B) The no observed effect levels (NOELs) from subchronic dermal and/or subchronic inhalation studies.

(ii) The toxicity data used for this determination should be that which gives the lowest AEL.

(2) **Use of data from other studies**. When NOELs from studies such as subchronic neurotoxicity, teratogenicity, and reproduction are lower than NOELs from subchronic dermal and/or inhalation studies, the data from the studies yielding the lower NOELs should be used to determine the AEL.

(3) **Conversion of toxicity data from oral routes to dermal routes.** The following considerations may be helpful if it is necessary to convert toxicity data obtained from animals dosed by oral route to approximate absorbed dermal dose.

(i) Comparison of acute oral LD50 and acute dermal LD50 (see OPPTS 870.1100 and 870.1200).

(ii) Physical state of the pesticide when exposure is expected (e.g. liquid, dust, granular, or encapsulated residues).

(iii) Actual dermal absorption data from experimental animal studies with the same or analogous chemicals.

(4) **Absorption.** For estimating penetration of pesticides through skin, the applicant may either assume l00 percent absorption or submit data including, but not limited to, that described in paragraph (b) of this guideline, to indicate that absorption is less than 100 percent. For penetration of pesticides through lung surfaces, the Agency will assume l00 percent penetration unless adequate data are submitted by the applicant to indicate otherwise.

(h) **Determining the AEL**—(1) **When required**. An AEL for each active ingredient in an end-use product is required to support the registration of each end-use product for which a reentry interval is required by 40 CFR 158.390 and discussed in paragraph (b)(1) of this guideline.

(2) **Determining the AEL.** The procedure used to determine an AEL will depend on the kinds of toxic effects produced by the active ingredient and on the extent of absorption. If the active ingredient does not produce oncogenic effects, the AEL should be determined using the guidance and considerations in paragraph (h)(2)(ii) of this guideline. Applicants may determine an AEL using other means and submit supporting data for the approach.

(i) **Nononcogenic substances.** The no observed effect levels (NOELs) discussed in paragraph (b)(2) of this guideline should be divided by an appropriate safety factor to determine the AEL. This safety factor should reflect the degree or amount of uncertainty to be considered when experimental data in animals are extrapolated to effects on man. Safety factors may vary from 10 to 2,000 and should reflect the nature of the toxicity (severity and reversibility), the length of the exposure, and the comparability (if known) between the animal and humans for pesticide absorption, distribution, excretion, and metabolic transformations. The NOELs from subchronic dermal or the allowable levels of human exposure. However, when a NOEL from studies such as subchronic neurotoxicity, teratology, and reproduction are lower, the NOEL derived from these studies should be used. If the animal studies are those which do not yield a NOEL, then appropriate levels of risk should be used to determine an AEL.

(ii) **Oncogenic substances.** The AEL for oncogenic substances should be based on a risk assessment using appropriate mathematical models applied to data derived from life-time animal studies. The applicant may determine an AEL using other means but should submit data to support the approach. The Agency can provide instructions for risk assessment and for calculation of the AEL.

(3) **Reporting of AEL.** (i) If the end-use product contains more than one active ingredient, the lowest AEL should be reported.

(ii) The AEL should be expressed in terms of daily dermal dose (such as milligrams per kilogram per day) or, in the case of airborne residues, in terms of airborne concentrations (such as milligrams per cubic meter).

(iii) The report on the calculation of the AEL should indicate the data used, any safety factor used, the mathematical model (if any), and the reasons for selecting each.

(i) **References.** The following references should be consulted for additional background material on this test guideline.

(1) Abrams, H.K. and A.R. Leonard, Toxicology of organic phosphate insecticides. *California Medicine* 73:183 (1950).

(2) Gunther, F.A., and J.D. Gunther (eds.). Minimizing occupational exposure to pesticides. *Residue Reviews* Volume 75 (1980). (This entire volume constitutes the proceedings of a conference on reentry and contains a number of papers on various topics underlying the prevention of field worker poisonings.)

(3) Gunther, F.A. et al., The citrus reentry problem: Research on its causes and effects, and approaches to its minimization. *Residue Reviews* 67:1–139 (1977). (This review is recommended as a starting point for information on the reentry problem and for references to research on the subject up to l977. The literature review is exhaustive and the index is useful.)

(4) Ingram, F.R., Health hazards associated with use of airplanes for dusting crops with parathion. *American Industrial Hygiene Association Quarterly* 12:165 (1951).

(5) Iwata, Yutaka et al., Fruit residue data and worker reentry research for chlorthiophos applied to California citrus trees. *Journal of Agricultural Food Chemistry* 30:215–222 (1982).

(6) Kahn, E., Outline guide for performance of field studies to establish safe reentry intervals for organophosphate pesticides. *Residue Reviews* 70:27–43 (1980).

(7) Kilgore, W.W. et al., Human physiological effects of organophosphorus pesticides in a normal agricultural field labor population. A preliminary report. II. Scientific aspects. Food Protection and Toxicology Center, University of California, Davis, CA (1977).

(8) Milby, T.H., Prevention and management of organophosphate poisoning. *Journal of the American Medical Association* 216:2131 (1971).

(9) Popendorf, W., Exploring citrus harvesters' exposure to pesticide contaminated foliar dust. *American Industrial Hygiene Association Journal* 41:652–659 (1980).

(10) Popendorf, W.J. and J.T. Leffingwell, Regulating OP pesticide residues for farmworker protection. *Residue Reviews* 82:125–201 (1982).(This paper contains a review of the literature as support for the authors' suggested model for the calculation of reentry intervals.)

(11) Quinby, G.E. and A.B. Lemon, Parathion residues as a cause of poisoning in crop workers. *Journal of the American Medical Association* 166:740 (1958).

(12) Task Group on Occupational Exposure to Pesticides, Federal Working Group on Pest Management. 1974. Occupational Exposure to Pesticides. U.S. Environmental Protection Agency, Washington, D.C. 20460. (This reviewcontains a history and discussion of the problem of fieldworker poisonings with organophosphorus pesticide residues on crops up to l974.)